

Exhibit A

Everett Infectious Diseases, PLLC

George Diaz, MD
Expert Witness in Infectious
Diseases

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Christopher F. Jeu
Assistant United States Attorney
United States Attorney's Office
District of New Mexico
(505) 224-1458 (direct)
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April 3, 2017

Dear Christopher Jeu, Assistant US Attorney,

You have asked me to review the medical records and other documents regarding Ms. Laura Jean Joe-Cruz, who has filed suit against the United States for alleged medical negligence in January 2014. Please find my expert report that documents my opinions regarding the treatment rendered.

Background Facts

Ms. Joe-Cruz is a Native American female aged 46 in January 2014.

In 2013, she declined influenza vaccination offered by the Canoncito Health Center on two separate occasions.

On January 7, 2014, there is an entry in the medical record indicating that the patient initially checked in to the clinic, but left before she was seen by a medical provider on that day.

On January 9, 2014, the original complaint's exhibit includes Supplement 1 of plaintiff's administrative claim. That includes Ms. Joe-Cruz's description of medical care provided on January 9 that she was told she had influenza, to increase fluid intake and to use Tylenol. There is no evidence in the medical record that Ms. Joe-Cruz saw a provider on that day.

The patient first saw a medical provider based on review of the medical record for respiratory symptoms in the clinic on January 10th, 2014. At that visit, she complained of symptoms beginning on

January 7th 2014. Based on both the recorded history taken from the patient and when the patient presented on January 10th, greater than 48 hours must have passed from when symptoms began and when she was evaluated initially by a provider on January 10th, 2014.

At the time the patient presented on January 10th, 2014, she had a normal blood pressure, normal respiratory rate, normal temperature, and was tachycardic. She also complained of sputum production. She was diagnosed with bronchitis and treated with Azithromycin.

Summary of Opinion

Part A. Treatment of influenza

Standard of care is defined at the local level by the communities that the provider serves. Practice guidelines such as provided by the CDC and IDSA are useful but do not define the standard of care. Practice guidelines clearly indicate that the clinical judgement of the provider is key and that it supersedes guidelines. Additionally, large health systems can apply restrictions to certain therapies based on cost effectiveness of those treatment modalities. As examples, Medicaid restricts treatment for patients that have Hepatitis C and Medicare restricts certain medications for treatment of C. difficile infection. Private insurance companies tier their pricing of medications so as to restrict utilization of certain expensive medications. Hospitals restrict their formularies to decrease the cost of health care. The Indian Health Service has conferred a non-formulary status to Tamiflu (trade name for Oseltamivir). This is based on a cost benefit analysis which is based on review of available data, which will be discussed below. For the individual provider, the determination to use a certain treatment modality involves complex decision making, including patient characteristics, the prevalence of the disease in the community, in this case influenza, national and local guidelines, review of the evidence for benefit to the patient, as well as whether the treatment is readily available. All these issues make the standard of care a local decision, and not simply a recitation of national guidelines.

Options for treatment of influenza include basic treatments such as rest, fluids, and antipyretic agents such as Tylenol, as well as medications such as Oseltamivir, Zanamivir, and Peramivir. The benefit to using these agents has been shown to be a reduction in the symptoms of influenza by 15-24 hours. Based on this data, the FDA approved the use of Oseltamivir. The Tamiflu package insert includes the following statement: TAMIFLU is indicated for the treatment of acute, uncomplicated illness due to influenza A and B infection in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours. (<http://www.tamiflu.com/hcp/>). The package insert also includes language that says Tamiflu has not been shown to prevent complications [such as serious bacterial infections]. Additionally, the Physician Desk Reference also does not list indications for usage in patients with

symptoms greater than 48 hours. Furthermore, section 8.8 indicates that the efficacy of Tamiflu in patients with chronic cardiac and/or respiratory disease was not established. No clinical trial data are available regarding treatment of influenza in patients with any medical condition sufficiently severe or unstable to be considered at imminent risk of requiring hospitalization. In 2014, two large studies were published that reviewed all available randomized controlled studies regarding the use of Oseltamivir and Zanamivir in the treatment of influenza, which were sponsored by the Cochrane review. Firstly, the benefit of Oseltamivir was found to be about a 15 hour reduction in the time to improvement of influenza symptoms, which is similar result of just using Tylenol. More importantly, there was no evidence for reduction in the risk of complications of influenza, including pneumonia, hospitalization or death. Nor was there any evidence found for these possible benefits in children or adults considered at high risk. The drug manufacturer has been accused of publication bias, since the studies that led to FDA approval were drug company sponsored studies and possible negative studies have never been released, despite calls for them to do so.

(<https://www.forbes.com/sites/harlankrumholz/2013/01/08/the-myth-of-tamiflu-5-things-you-should-know/#29a7334b5782>)

Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. Jefferson T, Jones M, Doshi P, Spencer EA, Onakpoya I, Heneghan CJ BMJ. 2014;348:g2545.

Zanamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. Heneghan CJ, Onakpoya I, Thompson M, Spencer EA, Jones M, Jefferson T BMJ. 2014;348:g2547.

Part B. Influenza vaccination

Prevention of influenza by vaccination is universally recognized as the best way to prevent the complications that may arise as a result of infection with influenza. This is in stark contrast to the modest benefit of Tamiflu, discussed above. In addition, the influenza vaccine that was available for the 2013-2014 season was quite effective with a greater than 60% reduction in medical visits for influenza, meaning that the disease was prevented in the majority of patients

(<https://www.cdc.gov/mmwr/pdf/wk/mm6307.pdf>). Unfortunately, in this case, vaccinations including influenza were offered to, but declined by the plaintiff twice in 2013. Had the plaintiff been compliant with clinic recommendations, it is more likely than not that her entire illness would have been avoided. At the time the patient presented to the Canoncito Health Center in January 2014, influenza vaccination was not appropriate to administer because protective antibody response takes 2 weeks to develop in the majority of adults and would not have prevented the infection with influenza in this

patient.

(https://www.cdc.gov/mmwr/volumes/65/rr/rr6505a1.htm?s_cid=rr6505a1_w#timing_vaccination).

Part C. Guidelines regarding the use of Oseltamivir

The 2009 IDSA guideline provides an overview of the strength of recommendations as follows (taken from table 1):

Category, grade Definition
 Strength of recommendation
 A Good evidence to support a recommendation for or against use
 B Moderate evidence to support a recommendation for or against use
 C Poor evidence to support a recommendation
 Quality of evidence
 I Evidence from _1 properly randomized, controlled trial
 II Evidence from _1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from 11 center); from multiple time-series; or from dramatic results from uncontrolled experiments
 III Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

The 2009 IDSA guidelines have essentially 3 sets of patient populations where antiviral treatment is recommended, though clearly the evidence that supports treatment is weakest in the third group as noted below. The plaintiff's case falls within the third group where there is no clear benefit found in clinical trials (as described in section A) and the recommendation for treatment is based entirely on expert opinion.

1. Those patients that have symptoms and present within 48 hours of symptom onset. Based on the above data, there appears to be a benefit to treatment, albeit modest. The recommendation is based on data felt to be class A1, which is good evidence based on multiple randomized double blinded controlled trials.
2. Those patients who are hospitalized, and have symptoms less than 48 hours is A2 (good evidence based on well-designed clinical trial) or greater than 48 hours, which is B2 (moderate evidence based on well-designed clinical trial).
3. Those outpatients who are at high risk of complications, who are not improving, and have a positive influenza test 48 hours past onset of symptoms is C3, which is based on poor evidence and relies on expert opinion.

The CDC influenza guideline does not include language that requires a positive flu test for treatment of patients at high risk of complications to recommend treatment, including those patients that present greater than 48 hours after the onset of symptoms. The CDC also does not grade the evidence behind the recommendation in this setting. It is clear, however, that the evidence supporting this recommendation is weak. (CDC 2013-2014 Antiviral Medications: Summary for Clinicians)

Part D. Risk factors

The CDC guideline also lists risk factors that confer risk for complications associated with influenza infection. The studies cited to provide these recommendations are based on relatively poor evidence. A large meta-analysis was performed and published in 2013 which evaluated all available data regarding published risk factors. Risk factors that appeared to be important risk factors were obesity and the post-partum period. Obesity was a risk factor but is also associated with numerous other health issues which the authors noted could have confounded the association. Notably, ethnicity, including Native Americans, did not appear to confer increased risk for complications from influenza.

Populations at risk for severe or complicated influenza illness: systematic review and meta-analysis
Mertz et al. BMJ 2013;347:f5061

Part E: Influenza in New Mexico at the time the plaintiff presented to Canoncito Health Center

The percentage of patients presenting to clinics in the Northwest Region of New Mexico the week the patient presented had very small numbers of patients presenting with influenza-like-illness (roughly 3% of all patients), meaning that the Canoncito Health Center was not seeing much influenza the week that the patient presented with symptoms, although influenza was active in much of New Mexico (6-7%). (<https://nmhealth.org/data/view/infectious/79/>).

Part F. Influenza testing at Canoncito Health Center

Influenza testing was performed in the clinic on January 10th by nasal swab and was negative. The flu test that was used was the Sophia Quidel Flu A and B test nasal swab. This test detects 2009 H1N1 influenza and the product insert indicates a sensitivity of 78-99%, which includes the flu strain that was predominant in New Mexico in January 10th 2014. (<https://www.quidel.com/immunoassays/rapid-influenza-tests/sofia-influenza-fia>). Since the prevalence of influenza in the Northwest region of New Mexico was low, the negative predictive value of the test would have been good. (2009 IDSA Influenza guideline, table 5, *ibid.*)

Case review

The patient initially presented on January 7th, but left before being seen. The patient claims that she was seen by a medical provider on January 9th, and claims to have been told she had influenza, and that she was advised to increase fluid intake and to take Tylenol for symptom relief, which is a standard treatment for influenza like illness.

At the visit on January 10th, 2014, the patient was not generally a candidate to receive Tamiflu because greater than 48 hours had elapsed between the time she began complaining of symptoms and the time she saw a medical provider. Current guidelines recommend starting Tamiflu within 48 hours of the onset of influenza like illness. The benefit of starting Tamiflu beyond 48 hours of symptoms is not clear and the recommendations for treatment is based on poor evidence. Clinical judgement is important when deciding whether or not to begin antiviral treatment.

(<https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6001a1.htm>). Even treatment within 48 hours with Tamiflu has limited clinical benefit, merely reducing time to symptom relief by 15-24 hours. At most, it may have reduced the hospital stay by 1-2 days had she received Tamiflu on either January 7th or January 9th, 2014. Moreover, there is no evidence that administration of Oseltamivir would have prevented any associated complications including disability or loss of earnings.

The 2009 Infectious Diseases Society of America (IDSA) guideline on treatment of influenza indicates that treatment may be considered (note-not recommended by IDSA guidelines, simply that a provider can consider treatment) in patients who present greater than 48 hours of symptoms if they have lab proven influenza and are at high risk of complications. Although the patient had risk factors for complications from influenza, she had a documented negative influenza test. If the provider were to follow current IDSA guidelines at the time of the visit on Jan 10th, the provider would not have started Tamiflu. (http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Infuenza.pdf)

When the patient presented on January 10th, she demonstrated sputum production, which is not a common symptom in influenza and more commonly seen with bronchitis. This made an alternate diagnosis reasonable.

Lastly, the patient had near normal vital signs and discharge to home was a reasonable disposition. The patient had no findings at the clinic visit that suggests referral to the emergency room and admission was necessary. The patient was 3 days into her illness on January 10th, 2014. Had a diagnosis of influenza been made, it would have been reasonable to observe her since most cases of influenza resolve on their own within 3-7 days.

Based on clinical judgement, the patient had numerous reasons for not receiving additional treatment at the visit of January 10th 2014. In my opinion, standard of care was not breached as it relates to treatment of possible influenza in this patient. It was reasonable not to commence Tamiflu at that visit. Based on current available clinical studies, it is clear that Tamiflu is not a miracle drug and would not have cured the patient overnight. These opinions are expressed to a reasonable degree of medical probability.

Conclusions

- 1) Influenza vaccination more likely than not would have prevented the plaintiff's illness, but she was non-compliant with recommended vaccinations by Canoncito Health Center in 2013
- 2) An alternate diagnosis seemed likely based on the presence of sputum production on January 10th and treatment for bronchitis was reasonable
- 3) Influenza activity in the local area appeared to be low based on patients presenting to the clinic the week the patient presented, which would improve the negative predictive value of the flu test.
- 4) Influenza testing was done in the clinic and was negative.
- 5) Greater than 48 hours had passed of symptoms before her initial presentation to a medical provider and the patient did not appear to have progressive or severe disease based on near normal vital signs. She did not appear to require referral to an emergency for admission based on her clinical presentation that day. Treatment of patients with Tamiflu who present greater than 48 hours after the onset of illness has not been shown to decrease complications of influenza, including hospitalization or death.
- 6) The published risk factors for complications due to influenza are based on weak evidence.
- 7) Had the patient received Tamiflu on January 7th or 9th, at most, her hospitalization would have been shortened by 1-2 days.

I reserve the right to amend or supplement this report based upon ongoing discovery.


My qualifications are listed in the attached CV.

The only other case where I have testified by deposition is: Estate of Michael Lee Vincent, Sr., deceased, Plaintiff vs. SNOHOMISH COUNTY, a municipal corporation and/or a political subdivision of the State of Washington NO. 13 2 00368 9. I was deposed as a witness by the plaintiff in the case as I attended the patient. The defense did not dispute my status as an expert in Infectious Diseases and did not call any additional Infectious Diseases expert.

My rate for this case is \$400/hour for review of the case and report and \$550/hour if court testimony is required.

Respectfully,

George Diaz, MD


4/17/17

GEORGE A. DIAZ

TRAINING

2003-2005	University of Washington	Seattle, Washington
<i>Infectious Diseases Fellow</i>		
2002-2003	University of Utah	Salt Lake City, Utah
<i>Chief Medical Resident</i>		
1999-2002	University of Utah	Salt Lake City, Utah
<i>Resident in Internal Medicine</i>		
1995-1999	University of Oklahoma	Oklahoma City, Oklahoma
<i>M.D. May 1999</i>		
1989-1994	University of Washington	Seattle, Washington
<i>B.S. Microbiology</i>		

PUBLICATIONS

Jack J. Brandabur, MD, James E. Leggett, MD, Lian Wang, MS,
Rebecca L. Bartles, MPH, CIC, Lynda Baxter, MPH, MBA, George A.
Diaz, MD, Gary L. Grunkemeier, PhD, Shannan Hove, RN, Margret
Oethinger, MD, PhD
Surveillance of guideline practices for duodenoscopy and linear
echoendoscopy reprocessing in a large healthcare system
Gastrointestinal Endoscopy 2016 03:1480

Diaz, GA and Koelle DM
Human CD4+ CD25high cells suppress proliferative memory
lymphocyte responses to herpes simplex virus type 2
Journal of Virology 2006 Aug;80(16):8271-3

Diaz GA, Rakita RM, and Koelle DM
A case of HSV-2 Ramsey Hunt
Clinical Infectious Diseases 2005 May 15;40(10):1545-7

Chapter 5: Antiviral Agents including Antiretrovirals
Blueprints in Infectious Diseases
Blackwell Publishing 2006

EXTRACURRICULAR ACTIVITIES

2007-present Section Chief, Infectious Diseases, Providence Regional Medical Center Everett

2007-present Member, Infection Control Committee, Providence Regional Medical Center

2008-present: Co-chair, Pharmacy and Therapeutics, Providence Regional Medical Center Everett

2008-present Medical Director for PRMCE Antimicrobial Stewardship Program

2015-present Providence Health System Provider Informaticist, Infectious Diseases, a project to standardize the delivery of infectious diseases care as it relates to the electronic medical record.

2010-2014 Co-Chair, Clinical Advancement Team, Infectious Diseases, a project to standardize infectious diseases medical care across Providence Health and Services, including antimicrobial stewardship

2010-2014 Co-Chair, Safe Medication Formulary Workgroup/System Formulary Council, a project to standardize formularies across Providence Health and Services. Achievements include: Greater than 450 formulary determinations, 38 therapeutic interchanges, 150 medication groups created for use in Epic order set build, Standardizing strategies for: Anticoagulation reversal, Drug desensitization protocols, Best Practice Alerts, and Drug shortage mitigation

2011-present Lecturer for UW medical students

2012-present Medical Director for SAFE program, a program which transitions patients with infections and IV drug use to outpatient setting. Estimated savings \$1.3 million in direct hospital costs.

2013-present Member, PRMCE sepsis work group

Housestaff Committee, University of Utah, 1999-2001

Hispanic Student Association, President 1998-1999, Vice-President 1997-1998, Secretary/Treasurer 1996-1997. Various projects included organizing yearly Health Fairs for the Hispanic Community in Oklahoma City; running a low income clinic for Hispanics.

Class Treasurer 1997-1998 projects include organizing fund raising projects.

Medical Student Council- Organizational Representative 1996-1998

Dean's Curriculum Committee 1997 worked with faculty to give feedback on content and focus of 2nd and 3rd year coursework.

Medical School Admissions Committee 1998-1999

EMPLOYMENT

2016-present Antimicrobial Stewardship Services, PLLC (owner)

2015-present Everett Infectious Diseases, PLLC (owner)

2005-2014 Providence Medical Group Everett, Washington Infectious Diseases Staff Physician

2002-2005 Medical Officer of the Day, Fort Harrison Veteran's Administration, Helena, Montana

2001-2003 Social Security Disability Examinations, Johnsen Health Service, Salt Lake City, UT

1992-1995 Research Assistant, Preceptor: Christopher B. Wilson, MD

1994 Summer Fellow Worked at Sea-Mar Clinic, a free clinic in a mainly Hispanic community in South Seattle. Preceptor-Anthony Pedroza, MD. Formulated questionnaire and interviewed 100 patients to determine obstacles to health care in clinic's patient population. Results presented to Sea-Mar staff and at End of Fellowship Conference.

1991 Student Assistant, March of Dimes. Worked collecting data in the State of Washington regarding Pre-term births, Low Birth Weight Newborns, and Prenatal Care. Results used to determine allocation of funds to counties for Prenatal Health Care programs.

1990 Research Assistant, Harborview Medical Center, Seattle, Washington Collected data regarding helmet use among children in King County Parks

HONORS

2011 President's Award recipient, Providence Health and Services' highest award for improvement in healthcare for Antimicrobial Stewardship implementation at Providence Regional Medical Center Everett

2011 Qualis Health Awards of Excellence recipient, for improvement of patient safety and health at Providence Health and Services

2011 Pharmacy Resource Council Award recipient for Antimicrobial Stewardship, Providence Health and Services

Outstanding Intern of the Year, University of Utah, Department of Medicine, 1999-2000

Walter Mason Scholar 1999, University of Oklahoma

Outstanding Hispanic Student of the year 1999, University of Oklahoma
Health Sciences Center

Medical Student Service Award 1999, University of Oklahoma